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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
10/574,675	04/04/2006	Dennis Lee	PU60526	4093	
	7590 04/02/200 BEECHAM CORPOR		EXAM	UNER	
CORPORATE	RPORATE INTELLECTUAL PROPERTY-US, UW2220 RAHMANI, NILOOF		NILOOFAR		
P. O. BOX 153 KING OF PRU	9 ISSIA, PA 19406-0939		ART UNIT	ART UNIT PAPER NUMBER	
	,		1625		
			NOTIFICATION DATE	DELIVERY MODE	
			04/02/2008	ELECTRONIC	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Application No. Applicant(s) 10/574,675 LEFETAL

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Office Action Summary	Examiner	Art Unit					
	NILOOFAR RAHMANI	1625					
- The MAILING DATE of this communication appears on the cover sheet with the correspondence address							
Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA - Extensions of time may be available under the provisions of 37 CFR 1.15 after SIX (6) MONTHS from the mailing date of the communication. If IN Operiod for reply is specified above, the maximum statutory period to Failure to reply within the set or extended period for reply will by statute, Any reply received by the Office later than three months after the mailing carned patnet term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be tim- rill apply and will expire SIX (6) MONTHS from cause the application to become ABANDONE!	I. lely filed the mailing date of this c (35 U.S.C. § 133).					
Status							
1) Responsive to communication(s) filed on 04 Ag	oril 2006.						
	action is non-final.						
3) Since this application is in condition for allowar	Since this application is in condition for allowance except for formal matters, prosecution as to the merits is						
closed in accordance with the practice under E	closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.						
Disposition of Claims							
4) Claim(s) 1-7 is/are pending in the application. 4a) Of the above claim(s) is/are withdrav 5) Claim(s) is/are allowed. 6) Claim(s) 1-7 is/are rejected. 7) Claim(s) is/are objected to. 8) Claim(s) are subject to restriction and/or							
Application Papers							
9) The specification is objected to by the Examinei 10) The drawing(s) filed on is/are: a) acce Applicant may not request that any objection to the or Replacement drawing sheet(s) including the correction 11) The oath or declaration is objected to by the Ex	epted or b) objected to by the E drawing(s) be held in abeyance. See ion is required if the drawing(s) is obj	37 CFR 1.85(a). ected to. See 37 C					
Priority under 35 U.S.C. § 119							
12)⊠ Acknowledgment is made of a claim for foreign a)⊠ All b)□ Some * c)□ None of: 1.⊠ Certified copies of the priority documents 2.□ Certified copies of the priority documents 3.□ Copies of the certified copies of the prior application from the International Bureau * See the attached detailed Office action for a list of the prior application from the International Bureau	s have been received. s have been received in Applicati- ity documents have been receive I (PCT Rule 17.2(a)).	on No ed in this National	Stage				
Attachment(s)							
Notice of References Cited (PTO-892) Notice of Draftsperson's Patent Drawing Review (PTO-948)	Interview Summary Paper No(s)/Mail Da	(PTO-413) ite					

5) Notice of Informal Patent Application Information Disclosure Statement(s) (PTO/S5/c8)
 Paper No(s)/Mail Date 04/04/2006. 6) Other: U.S. Patent and Trademark Office PTOL-326 (Rev. 08-06)

Page 2

Application/Control Number: 10/574,675

Art Unit: 1625

DETAILED ACTION

Claims 1-7 are pending in the instant application.

2. Priority

This application was filed on 04/04/2006, which is a 371 of PCT/US04/32825, filed on 10/06/2004, which claims priority of UNITED STATES OF AMERICA 60/508,893, filed on 10/06/2003 and UNITED STATES OF AMERICA 60/532.085. filed on 12/23/2003...

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the

Application/Control Number: 10/574,675 Page 3

Art Unit: 1625

amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to method of inhibiting Rho-kinases using an effective amount of a compound according to claim 1.

The state of the prior art: "Y-27632 could prevent the inhibition of myosin light chain phosphatase via the Rho/ROCK-mediated signaling pathway. Y-27632 attenuates the methacholine-induced precontraction and potentiates the relaxant effects of B2-adrenoceptor agonists in bovine tracheal smooth muscle preparations. Therefore, not only a ROCK inhibitor alone but also its combination with B2-adrenoceptor stimulants may become a useful clinical strategy to improve airflow limitation in asthma." (Nakahara et al., European journal of pharmacology, 2000, Vol. 389, No. 1, pp. 103-6).

Art Unit: 1625

The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be used for inhibiting Rho-kinases.

Amount of guidance/working examples: On page 34-35 of the specification, applicant has example of ROCK inhibiting activity test compounds. However, the specification does not seem to enable the activity of compounds to a disease such as cancer, stroke, asthma and etc.

Page 5

Application/Control Number: 10/574,675

Art Unit: 1625

The breadth of the claims: The breadth of claims is drawn to a method of inhibiting Rho-kinases using an effective amount of a compound according to claim1.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for inhibiting Rhokinases, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 3-6, for inhibiting Rho-kinases, have been enabled by the instant specification.

4. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

Page 6

Application/Control Number: 10/574,675

Art Unit: 1625

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 35(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, and 8-15 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Bailey et al., WO 03/080610. Bailey et al. disclosed the instant claimed compounds and compositions, which from the STN search are

RN 607369-14-2 CN 1H-Imidazo[4,5-c]pyridine-1-ethanamine, 2-(4-amino-1,2,5-oxadiazol-3-v))- N.N.b-trimethyl-

RN 607369-34-6

Art Unit: 1625

CN 1,2,5-Oxadiazol-3-amine, 4-[1-(3-piperidinyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

RN 607369-25-5

CN 1H-Imidazo[4,5-c]pyridine-1-ethanamine, 2-(4-amino-1,2,5-oxadiazol-3-yl)- N,N,b-trimethyl-, (+)

H2M H

RN 607369-27-7

CN 1H-Imidazo[4,5-c]pyridine-1-ethanamine, 2-(4-amino-1,2,5-oxadiazol-3-yl)- N,N,b-trimethyl-, (-)-

, RN 607369-37-9

Art Unit: 1625

CN 1,2,5-Oxadiazol-3-amine, 4-[1-(3-piperidinyl)-1H-imidazo[4,5-c]pyridin-2-yl]-,

RN 607369-38-0

CN 1,2,5-Oxadiazol-3-amine, 4-[1-(3-piperidinyl)-1H-imidazo[4,5-c]pyridin-2-yl]-,

RN 607369-19-7

CN Carbamic acid, [4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1H-imidazo[4,5-c]pyridin-1-yl]butyl]-, 1,1-dimethylethyl ester

,

Art Unit: 1625

RN 607369-40-4 CN 1,2,5-Oxadiazol-3-amine, 4-[1-(4-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

RN 607369-43-7 CN 1,2,5-Oxadiazol-3-amine, 4-[1-(4-aminophenyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

RN 607369-45-9 CN 1,2,5-Oxadiazol-3-amine, 4-[1-(3-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

,

Art Unit: 1625

RN 607369-53-9 CN 1,2,5-Oxadiazol-3-amine, 4-[1-(3-bromophenyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

RN 607369-54-0

CN Phenol, 4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1H-imidazo[4,5-c]pyridin-1-yl]-

RN 607369-73-3

CN 1,2,5-Oxadiazol-3-amine, 4-[1-[4-[(methylthio)methoxy]phenyl]-1H- imidazo[4,5-c]pyridin-2-yl]-

Art Unit: 1625

RN 607369-75-5 CN 1,2,5-Oxadiazol-3-amine, 4-[1-[4-[(phenylthio)methoxy]phenyl]-1H- imidazo[4,5-c]pyridin-2-yl]-

RN 607369-77-7 CN Carbamic acid, [2-[4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1H-imidazo[4,5-c]pyridin-1-yl]phenoxy]ethyl]-, 1,1-dimethylethyl ester, trifluoroacetate

RN 607369-88-0

CN 1,2,5-Oxadiazol-3-amine, 4-[1-[4-(2-aminoethoxy)phenyl]-1H-imidazo[4,5-c]pyridin-2-yl]-, hydrochloride

, RN 607370-41-2

CN 1,2-Ethanediamine, N'-[4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1H-imidazo[4,5-c]pyridin-1-yl]phenyl]-N,N-dimethyl-

Art Unit: 1625

RN 607370-88-7

CN 1,2,5-Oxadiazol-3-amine, 4-[1-(1,2,3,4-tetrahydro-7isoquinolinyl)-1H- imidazo[4,5-c]pyridin-2-yl]-

RN 607370-99-0

CN 1,2,5-Oxadiazol-3-amine, 4-(7-bromo-1-ethyl-1H-imidazo[4,5c]pyridin-2-yl)-

RN 607371-24-4

CN 1,2,5-Oxadiazol-3-amine, 4-[1-ethyl-7-[4-(methylthio)phenyl]-

1H- imidazo[4,5-c]pyridin-2-yl]-

Art Unit: 1625

RN 607371-97-1

CN Benzaldehyde, 4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H-imidazo[4,5- c]pyridin-7-yl]-

RN 607372-01-0

CN 1-Piperidinecarboxylic acid, 4-[[[4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H-imidazo[4,5-c]pyridin-7-yl]phenyl]methyl]amino]-, 1,1-dimethylethyl ester

Application/Control Number: 10/574,675 Art Unit: 1625

RN 607372-09-8

CN Benzoic acid, 4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H-imidazo[4,5- c]pyridin-7-yl]-

RN 607372-10-1

CN Benzoic acid, 3-[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H-imidazo[4,5-c]pyridin-7-yl]-

Application/Control Number: 10/574,675
Art Unit: 1625

RN 607372-27-0 CN 1,2,5-Oxadiazol-3-amine, 4-(1-cyclopropyl-7-phenyl-1H-imidazo[4,5-c]pyridin-2-yl)-

RN 607372-33-8 CN 1,2,5-Oxadiazol-3-amine, 4-(7-bromo-1-phenyl-1H-imidazo[4,5-c]pyridin-2- yl)-

RN 607372-41-8 CN 1,2,5-Oxadiazol-3-amine, 4-[7-bromo-1-(4-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2-yl]- Application/Control Number: 10/574,675 Art Unit: 1625



RN 607372-42-9 CN Phenol, 4-[2-(4-amino-1,2,5-oxadiazol-3-yl)-7-bromo-1Himidazo[4,5-c]pyridin-1-yl]-

RN 607372-46-3 CN 1H-Imidazo[4,5-c]pyridine-7-methanamine, 2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-N-4-piperidinyl-

,

Art Unit: 1625

RN 607372-47-4

CN 1H-Imidazo[4,5-c]pyridine-7-carboxaldehyde, 2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-



RN 607372-99-6

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H-imidazo[4,5-c]pyridin-7-yl]methyl-8-methyl-

RN 607373-25-1

CN Piperazine, 1-[[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H-imidazo[4,5- c]pyridin-7-yl]carbonyl]-, dihydrochloride

RN 607373-28-4

Art Unit: 1625

CN Carbamic acid, [2-[4-[[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H- imidazo[4,5-c]pyridin-7-yl]carbonyl]-1-piperazinyl]ethyl]-, 1,1-dimethylethyl ester

t-Bu0-C-HH-CH2-CH2

RN 607373-29-5

CN Piperazine, 1-[[2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-1H-imidazo[4,5-c]pyridin-7-yl]carbonyl]-

RN 607373-40-0

CN 1H-Imidazo[4,5-c]pyridine-7-carboxamide, 2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-N-4-piperidinyl-, dihydrochloride

Art Unit: 1625

RN 607373-65-9 CN 1H-Imidazo[4,5-c]pyridin-7-ol, 2-(4-amino-1,2,5-oxadiazol-3-yl)-1-ethyl-

RN 607368-87-6 CN 1,2,5-Oxadiazol-3-amine, 4-(1-ethyl-1H-imidazo[4,5-c]pyridin-2-yl)-

RN 607368-93-4 CN 1,2,5-Oxadiazol-3-amine, 4-(1-cyclopropyl-1H-imidazo[4,5-c]pyridin-2-yl)-

Art Unit: 1625

RN 607368-95-6 CN 1,2,5-Oxadiazol-3-amine, 4-(1-methyl-1H-imidazo[4,5-c]pyridin-2-yl)-

RN 607368-97-8 CN 1,2,5-Oxadiazol-3-amine, 4-(1-cyclohexyl-1H-imidazo[4,5-c]pyridin-2-yl)-

Art Unit: 1625

RN 607368-99-0 CN 1.2.5-Oxadiaz

 ${\footnotesize CN~~1,2,5-Oxadiazol-3-amine,~4-[1-(cyclopropylmethyl)-1 H-imidazo[4,5-c]pyridin-~2-yl]-} \\$

, RN 607369-01-7

CN 1,2,5-Oxadiazol-3-amine, 4-[1-(cyclohexylmethyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

Art Unit: 1625

RN 607369-03-9 CN 1,2,5-Oxadiazol-3-amine, 4-(1-cyclobutyl-1H-imidazo[4,5-

c]pyridin-2-yl)-

RN 607369-05-1

CN 1,2,5-Oxadiazol-3-amine, 4-[1-(2-ethylbutyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

RN 607369-07-3

Art Unit: 1625

CN 1,2,5-Oxadiazol-3-amine, 4-[1-(1-methylethyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

RN 607369-09-5 CN 1,2,5-Oxadiazol-3-amine, 4-[1-(1-methylpropyl)-1H-imidazo[4,5-c]pyridin-2- yl]-

, RN 607369-11-9 CN 1,2,5-Oxadiazol-3-amine, 4-(1-cyclopentyl-1H-imidazo[4,5-c]pyridin-2-yl)-

RN 607369-41-5

Art Unit: 1625

CN 1,2,5-Oxadiazol-3-amine, 4-(1-phenyl-1H-imidazo[4,5-c]pyridin-2-yl)-

RN 607369-46-0 CN 1,2,5-Oxadiazol-3-amine, 4-[1-(2-methoxyphenyl)-1H-imidazo[4,5-c]pyridin-2-yl]-

RN 607371-09-5 CN 1,2,5-Oxadiazol-3-amine, 4-[1-ethyl-7-(2-thienyl)-1H-imidazo[4,5-c]pyridin- 2-yl]-

RN 607371-14-2

Art Unit: 1625

CN 1,2,5-Oxadiazol-3-amine, 4-[7-(3-ethoxyphenyl)-1-ethyl-1H-imidazo[4,5-c]pyridin-2-yl]-

. Therefore, the instant claim is anticipated by Bailey et al.

6. Claim Rejections - Obvious Double Patenting

Claims 1-7 are provisionally rejected under the judicially created doctrine obviousness-type double patenting as being unpatentable over the claims 1-4, 6-16, and 18 of Bailey et al., US 2005/0197328. Although the conflicting claims are not identical, they are not patentably distinct from each other because the current invention embraces the invention claimed in the above patent.

Determination of the scope and content of the prior art (MPEP §2141.01)

Bailey et al. claimed identical compounds, pharmaceutical composition and method of using the compounds in claims 1-4, 6-16, and 18, wherein X_3 being Nitrogen, X_1 being Carbon, X_2 being Carbon and X_1 being Carbon and X_2 being Oxygen and X_3 being Oxygen and X_4 being Nitrogen.

Ascertainment of the difference between the prior art and the claims (MPEP \$2141.02)

Page 27

Application/Control Number: 10/574,675

Art Unit: 1625

The difference between the instant claims and the issued claims is the claims are not word for word identical but the scope of both sets of claims overlaps mostly significantly with each other.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

The issued claims 1-4, 6-16, and 18 are therefore <u>fully embraced</u> by the instant claims 1-7.

This is provisional <u>obviousness-type</u> double patenting rejection because the conflicting claims have not in fact been issued.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, In re Thorington, 418 F.2d 528, 168 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b).

Effective January 1,1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867.

Page 28

Application/Control Number: 10/574,675

Art Unit: 1625

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI

D.MARGARET SEAMAN

03/24 /2008

PRIMARY EXAMINER

GROUP 1625

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625